CHAPTER 8

Allowing for the Effects of Associated Factors

The aim of the first of these more complex procedures is to compare the later performance of the children in the different groups after making due allowance for the 'confusing' effects of all the relevant associated factors for which we have sufficient information available. The most satisfactory technique for this purpose appears to be analysis of covariance. The 15 associated factors (covariates) which we have included in the first stage of this analysis are listed in Table 8.1. Most of them showed significant differences in distribution between the abnormal groups (and so might be suspected of causing 'confusing' distortions of the test results). However, in the case of the Eysenck Personality Inventory of the mother, in the interests of completeness we have included the extraversion score, for which there were no significant differences between the groups, as well as the neuroticism score, for which there were (see Table 2.5, p. 13).

Because of the extensive and detailed nature of our follow-up studies, a very large number of measures of performance is available to us. We have selected 13 for this analysis (see Table 8.2) so as to give as wide a cover as possible of the types of performance which we have investigated. We have carried out an analysis of covariance on each of these 13 measures (referred to as variates), in order to see whether the groups differ with respect to each of them, while allowing for the effects of all the covariates. Most of the variates we have included were found to distinguish between two or more of our groups in the simple types of analysis reported in earlier chapters. In the case of reading performance, however, neither of the tests administered showed any significant difference between the groups in the simple analyses (see Table 3.12, p. 32), but we consider it desirable to include a test of this important type of performance in this more complex analysis to see if the associated factors might in this case be masking a real difference between the groups.

Analysis of Covariance—First Stage

In this first stage we examined the standardised partial regression coefficients of each of the 15 covariates in each of the 13 analyses of covariance, in order to ascertain which of the covariates were individually important in relation to the 13 variates. The object of this stage is to eliminate from the second stage those associated factors (covariates) which are found not to have an important independent relationship with more than one or two variates: their exclusion therefore would not materially alter the results of the analyses. As a result of this reduction in the number of covariates, the results of the second stage of the analysis should be easier to interpret and understand. Also, a slightly greater number of children can be included in the second stage, since fewer have to be excluded because of incomplete information (concerning any of the covariates which are not included in the second stage).

TABLE 8.1

The 15 covariates used in the first stage of the analysis of covariance (see text)*

	Associated factors (covariates)	*Categories: no. and definition*	*Refer to Table No.*	*No. of important relationships*
	Biological			
a	Mother's age †	Continuous : years	2.2	6
b	Mother's height	Continuous : cm.	2.2	2
c	Mother's smoking	4 : 0, 1-5, 6-20, 20/day	2.2	1
d	Child's sex †	2 : boy, girl	2.2	3
	Clinical			
e	Antepartum haemorrhage †	2 : present, absent	2.2	5
f	Mode of delivery †	2 : breech, other	2.2	5
g	Delay in establishing regular respiration	3 : 1, 1-4, 5+ mins.	2.2	0
	Family			
h	Occupational class of father	5 : I, II, III, IV, V+	2.3	0
i	Mother's care of child at 3 years †	3 : good, doubtful, poor	2.4	6
j	Child's ordinal position in family †	Continuous : birth rank	2.4	7
k	Child read to	3 : no, occasional, regular	2.4	1
l	Relatives baby-sit	2 : yes, no	2.4	0
	Mother			
m	EPI — Extraversion	Continuous — score	—	2
n	EPI — Neuroticism	Continuous — score	2.5	0
o	Maryland — Rejection	Continuous — score	2.5	0

*These 'associated factors' are divided into four arbitrary groups: each is named, and information given about the number and definitions of the categories into which it was subdivided for the purposes of the analyses of covariance; with the number of the table in which its simple distribution is shown; and the number of variates with which it was found to have an important relationship.
†Factors with significant coefficients in relation to 3 or more variates (measures of performance — see Table 8.2)

The results of the first stage of the analysis of covariance are summarised in Table 8.1. It can be seen that there are only six of the associated factors (covariates) tested for which we have found an important relationship to three or more of the 13 measures of function (variates). We will be discussing the effects of these six factors in the second stage of the analysis, but only as a group, without attempting to distinguish their individual effects; so at this stage we would like to comment briefly upon the results summarised in Table 8.1, with reference to the individual covariates.

Among the biological factors it is not surprising to find that the mother's height and smoking habits produced few relevant coefficients. Any effect they might have had is likely to be mediated indirectly through their effects upon intra-uterine growth, and these effects are allowed for separately in this analysis. The mother's age, though a biological factor with well-recognised adverse effects of increasing years upon perinatal mortality, may also reflect differences in social environment, increasing maternal age being associated with favourable effects upon the subsequent performance of the survivors of the neonatal period (Illsley 1967). The child's sex is associated with well-recognised adverse effects upon perinatal mortality among boys;

TABLE 8.2
Adjusted mean scores of the children in our four groups, derived from the second stage analysis of covariance (see text) †

	Measures of performance (variates)	*Random control*	*Short gestation*	*Rather light-for-dates*	*Very light-for-dates*
	Tests where higher score favourable	(159) ‡	(53)	(56)	(67)
1	*WPPSI Verbal IQ at 6 years	100.5	96.9	97.0	94.7
2	**WPPSI Performance at 6 years	97.8	91.6	95.0	91.5
3	**ITPA Language Quotient at 7 years	98.6	93.5	94.2	91.8
4	Holborn Reading Quotient at 7 years	93.1	92.3	94.3	91.3
5	***Height at 7 years (cm)	121.9	119.7	120.5	117.8
6	**Weight increment, birth to 7 years (kg)	20.3	20.4	19.9	18.8
	Tests where lower score favourable				
7	*Bender-Gestalt Visuo-motor Errors	5.0	5.5	5.1	6.6
8	*Ozeretsky/Stott Motor Impairment	2.0	3.0	2.6	3.4
9	Behaviour abnormalities (mother)	37.1	38.0	36.4	39.2
10	Behaviour abnormalities (teacher)	4.6	4.5	5.0	5.2
11	*Activity-intensity abnormalities at 7 years (mother)	12.6	13.8	12.8	14.2
12	***Neurological abnormalities, 'soft'	12.7	13.8	13.4	14.3
13	***Neurological abnormalities, gesture	29.1	33.3	29.3	34.4

* = $p<0.05$ ** = $p<0.01$ *** = $p<0.001$ for F ratio (variance ratio) of scores for all four groups.

† The six covariates whose combined effects have been allowed for in deriving these scores are: mother's age; child's sex; antepartum haemorrhage; mode of delivery; quality of mother's care of child at age three years; child's ordinal position in the family. In items 1 to 6 a higher score is considered favourable (better performance); in items 7 to 13 a higher score is considered unfavourable (more abnormalities).

‡ The total number of children included in this analysis in each of our four groups, shown in brackets, is somewhat smaller than the totals shown in Chapter 1, because only those cases with complete information for all the 6 covariates and 13 variates could be included.

and the greater vulnerability of boys to adverse factors may also be reflected in impaired performance later, *e.g.* following breech delivery in the population from which our groups were selected (Neligan *et al.* 1974).

Of the 'clinical' factors, antepartum haemorrhage clearly involves a risk of anoxia (Walker 1959). Evidence for the harmful sequelae of breech delivery has been referred to above, and the high rate of breech delivery in our abnormal groups (see Table 2.2) would tend to strengthen the effect of this factor in our analysis. The fact that delay in establishing regular respirations had no important relationship with any of the 13 variates is consistent with the findings in the total population studied and reported by Neligan *et al.* (1974).

Of the 'family' factors, it may seem surprising to find that the father's occupational social-class provided no significant coefficients in view of the well-known effects of this factor upon many aspects of performances; these were strongly

confirmed in the parent population by Neligan *et al.* (1974). It seems likely that this finding in our present analysis is explained by the fact that most of the effects usually ascribed to the global and non-specific factor of 'social class' are accounted for by much more specific associated factors, such as the mother's standard of care of her child and the child's ordinal position in the family (which we have here classified as a social factor, although low birth-rank also has a biological effect, in the opposite direction, of increasing the risk of stillbirth (Illsley 1967)). This possibility was not fully investigated by Neligan *et al.* (1974), but it is considered in more detail in the next chapter. These two associated factors, and the mother's age, are the three covariates with the largest number of important influences in this analysis (Table 8.1). Neither the parents' concern with their child's language development (as reflected in the regularity with which they read to him), nor the amount of support they received from their own families (as gauged by the activity of baby-sitting) showed more than an isolated important relationship.

Among the maternal psychological factors tested in this analysis it is perhaps surprising to find that the rejection score of the Maryland Parent Attitude Scale showed no important relationships, in view of its very significant association with the short-gestation group in Table 2.5 (p. 13). On the other hand, the extraversion score in the Eysenck Personality Inventory, which showed no such association, produced two important relationships. It would seem that the tests used for quantifying maternal psychological factors in this study were not measuring qualities which produced important effects upon the children's performance, as we have assessed it.

Analysis of Covariance—Second Stage

The procedure employed allowed us to recalculate the mean score for each of the same 13 measures of performance (variates) in each of our four groups of children, after allowing for the combined effects of all the six associated factors (covariates) which produced three or more significant coefficients in the first stage. These were: mother's age, child's sex, antepartum haemorrhage, mode of delivery, quality of mother's care of child at age three years, and child's ordinal position in the family. The results are shown in Table 8.2 (the variates for which mean scores in the four groups differ significantly are indicated by one or more asterisks). This is so in the case of 10 measures of function, and only just fails to be so in the case of behaviour abnormalities derived from the mother's report ($p=0.056$). There is again no significant difference between our four groups in reading ability (as reflected by the Holborn Test), so this result in the simpler analysis (see Table 3.12, p. 32) is not altered by taking the six associated factors into account. There is also no significant difference between the four groups in terms of behaviour abnormalities, derived from the teacher's report using the Rutter Inventory, Scale B, when the effects of the six associated factors are allowed for in this analysis. This is in contrast to the simple analysis reported in Table 4.3 (p. 41) in which the proportion with an 'abnormal' score was significantly greater in the very light-for-dates than in the control group.

The tests of significance represented in Table 8.2 do not, of course, imply any value judgment: such judgments have to be made by eye from inspection of the mean

values shown. In 9 out of 10 items where there is a significan F ratio, the most favourable score (highest in 1 to 6, lowest in 7 to 13) is in the control group, the least favourable in the very light-for-dates, and the short-gestation group's score is intermediate. In the 10th item (weight increment from birth to seven years), the short-gestation group's score is virtually identical with the control group's, so that the variance ratio's significance in this case is all accounted for by the two light-for-dates groups. The rather light-for-dates group's score is more favourable than that of the very light-for-dates group for all 13 items and it is less favourable than that of the control group for all 10 items where the variance ratio is significant. It looks as if progressively greater impairment of the rate of intra-uterine growth still causes progressively greater impairment of performance, even when the six most important associated factors are allowed for.

These results of the two stages of the analysis of covariance simply serve to strengthen the general conclusions of the simpler analyses reported in the earlier chapters, that the children in both extreme abnormal groups perform less well than those in the control group. However, they do nothing to answer the clinically important question of whether being born very much too small (with a corrected birthweight in the lowest 5 per cent) is significantly more harmful than being born too soon (among the 5 per cent with the lowest gestational ages) when judged in terms of the children's performance at five to seven years of age. We have therefore directly compared the effects of these two adverse factors in a further analysis.

Direct Comparison of Extreme Groups

In this case we have repeated the type of analysis of covariance summarised in Table 8.2, except that we have included only the two extreme abnormal groups (short-gestation and very light-for-dates). We have allowed for the effects of the same six covariates as are listed in the heading of Table 8.2. As a result, we can directly compare the magnitude of the adverse effects of being born too soon (before 255 days gestation) with those of being born much too small (birthweight below the 5th centile) upon the same 13 variates, without the distorting effects of the other two groups of children included in Table 8.2. The results of this direct comparison are shown in Table 8.3. It is clear that all the differences in the scores or values are in the same direction as before (the results for the very light-for-dates being less favourable than those for the short-gestation group) but there is now only one statistically significant difference (in the weight increment from birth to seven years). There are also two borderline ones, for height at seven years ($p = 0.058$) and for the Bender-Gestalt test ($p = 0.054$).

However, the fact that the direction of every single one of these 13 differences, measuring a wide range of types of performance, is to the advantage of the short-gestation group, must surely be of significance in itself. In a further analysis of covariance we have tested this supposition by dichotomizing the scores of each of the 13 variates at the mean and adding these scores (0 or 1) together in order to compare the two groups. By this test the over-all difference between the performance of the two groups is highly significant ($p = 0.01$).

TABLE 8.3

Direct comparison of the mean scores of the children in the two extreme abnormal groups*

	Measures of performance (variates)	*Short gestation*	*Very light-for-dates*
	Tests where higher score favourable		
1	WPPSI Verbal IQ at 6 years	96.4	94.2
2	WPPSI Performance at 6 years	91.3	90.8
3	ITPA Language Quotient at 7 years	92.5	91.5
4	Holborn Reading Quotient at 7 years	91.8	90.3
5	Height at 7 years (cm)	119.6	117.9
6	**Weight increment, birth to 7 years (kg)	20.4	18.9
	Tests where lower score favourable		
7	Bender-Gestalt Visuo-motor Errors	5.5	6.7
8	Ozeretsky/Stott Motor Impairment	3.0	3.6
9	Behaviour abnormalities (mother)	37.9	39.4
10	Behaviour abnormalities (teacher)	4.9	5.5
11	Activity-intensity abnormalities at 7 years (mother)	14.0	14.2
12	Neurological abnormalities, 'soft'	13.9	14.5
13	Neurological abnormalities, gesture	33.3	34.7

*Derived from an analysis of covariance in which the combined effects of the same six covariates as in Table 8.2 were allowed for.
**$p<0.001$

Discussion

The general conclusion which we can draw from the results of the analyses of covariance reported in this chapter is that the results of the simpler analyses reported in Chapters 3 to 6 are remarkably little altered by making allowances for the results of our 15 'confusing' factors, subsequently reduced to the six important ones. The scores of the children who were born too soon are still depressed below those of the random control group; those of the children who were born very much too small are even further depressed; and those who were born rather too small have intermediate scores. Furthermore, if we simplify the picture and sharpen the focus upon the question of primary clinical importance, after allowing for the same six 'confusing' factors, we see (Table 8.3) that a direct comparison of the two extreme groups produces a result which is consistently in favour of those who were born too soon, their over-all advantage being highly significant ($p = 0.01$).

In making this direct comparison between the two extreme abnormal groups, we should bear in mind that the methods we used for selecting our study population (described in Chapter 1) tended to place the short-gestation group at a relative disadvantage. Firstly, we used the device of excluding from this group all children whose birthweight fell above the 90th centile (see Fig. 1, p. 5) as the only practical and objective means of eliminating the rather large number of children whose gestational age tends to be wrongly reported as less than 37 weeks in studies of large populations. In doing so we have to accept the loss from the short-gestation group of

children whose nett intra-uterine growth rate was greatest and who might therefore have been expected to perform best later on. Secondly, although the numbers of children in the two extreme abnormal groups (59 in the short-gestation, 74 in the very light-for-dates) were sufficiently similar to be described as 'comparable', the fact that there were actually fewer in the former group means that they represent a somewhat more extreme degree of the abnormality of shortening of the duration of intra-uterine growth than the latter group do of its nett rate. We have made no attempt to allow for the distorting effects of these selection factors, both of which must tend to the disadvantage of the short-gestation group. Had we been able to do so, presumably the relative inferiority of the very light-for-dates group in terms of later performance would have been even greater.

A further technical point which should be borne in mind, although we have no reason to believe that its effects will tend to favour one group at the expense of another, is that the list of 15 'confusing' factors we allowed for is very far from being comprehensive. We explained earlier that our information is relatively superficial and incomplete in certain areas (*e.g.* postnatal biochemical disturbance and details of calorie and fluid intakes); and even where it is most complete and precise we have had to be selective so as to keep the complexity of the analyses within reasonable bounds. For these reasons, and because of a basic ignorance concerning all the factors which determine a child's performance in a particular activity, the factors for which we have made allowance fall very short of accounting for all the variance in our children's performance, other than that which can justifiably be attributed to the differences between the groups themselves. The results reported in this chapter therefore cannot claim to be the final answer; we have not been able to eliminate the effects of all conceivable 'confusing' factors, but we have eliminated all those concerning which we have reliable information and which seem most likely to have a distorting effect upon the performance of the children in an abnormal group.

The extent to which these 15 factors, and three or four more which we have added to them in the analyses reported in the next chapter, do actually account for the variance of each group of children's scores in each of 13 tests of performance can be seen by looking at the bottom section of Figures 11 to 13 in the next Chapter. But the main purpose of those analyses will be to compare the relative magnitude of the effects of these 'confusing' factors. In the present chapter we have attempted to eliminate their effects, so as to allow us to compare the effects of the abnormalities of intra-uterine growth themselves as directly as possible. In the next chapter we will be looking at the effects of the 'confusing' factors themselves and comparing their magnitude within each type of measure of performance, within our various groups of children.